REMARKS

Claims 1-42, 48, and 51-60 have been cancelled. Claims 43, 67, and 68 have been amended. Claims 43-47, 49-50, and 61-69 are now pending in this application. Support for the amendments is found in the existing claims and the specification as discussed below. Accordingly, the amendments do not constitute the addition of new matter. Applicant respectfully requests the entry of the amendments and reconsideration of the application in view of the amendments and the following remarks.

Rejection under 35 U.S.C. § 102(b)

Claims 43-50, and 61-69 are rejected under 35 U.S.C. § 102(b) as being anticipated by Harris, et al. (WO 94/09131, published 4/94).

The Examiner states that Harris et al. teach molecules with CH1-VH and CL-VL domains associating and each of the domains CHI and CL, can have scFv linked to them with a peptide linker at the C-terminus and the molecules are trispecific, multispecific, bispecific, multivalent and pharmaceutical compositions.

Applicants have amended the claims to specifically recite that linkage is from the C-terminus of the dimerized Fab fragment to the N-terminus of the other molecule. Support for the amendment is found in cancelled claim 48. Applicants submit that Harris, et al. no longer anticipates the claims as amended.

Furthermore, Applicants assert that the present claims are not obvious in view of Harris et al. as Harris et al. do not teach or suggest fusion of scFv with the N-terminus to the C-terminus of the Fab chains. Indeed one of ordinary skill in the art at the time of the claimed invention would not know that efficient heterodimerization, which depends heavily on the S-S bridging at the C-terminus of the Fab fragment for stabilization of the heterodimer, could occur while a bulky molecule is attached at the C-terminus of both the CL and CH1 chains of the Fab fragment. Indeed, it was commonly known to those of ordinary skill in the art that the cysteine at the C-terminus of the CL chain should be freely available for efficient S-S bridging as is the case in natural antibodies or known derivatives. Thus, it was not predictable at the time of the claimed invention that efficient dimerization would be possible with a cysteine which is constrained because of being fused to a bulky molecule. Moreover, it would not have been obvious that fusing two molecules to the C-terminus of each of the Fab chains, which are only a few Angstroms apart from each other because of the disulfide bridge, would still lead to the

production of a molecule comprising a full activity of these molecules. This constraint is not present in fusion to the N-terminus of the Fab chains, where the N-terminal chain endings are separated relatively far away and on the opposite sides of the longitudinal axis of the molecule. Thus, based upon the state of the art at the time of the claimed invention, one of ordinary skill would not expect that fusion of molecules with the N-terminus to the C-terminus of a Fab fragment would be successful. Thus, Applicants submit that the present claims are patentable over Harris, et al.

In view of Applicants' amendments and arguments, reconsideration and withdrawal of this ground of rejection is respectfully requested.

CONCLUSION

In view of Applicants' amendments to the claims and the foregoing Remarks, it is respectfully submitted that the present application is in condition for allowance. Should the Examiner have any remaining concerns which might prevent the prompt allowance of the application, the Examiner is respectfully invited to contact the undersigned at the telephone number appearing below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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Dated: Dec. 15, 2003

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